BMJ Open

A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019160
Article Type:	Research
Date Submitted by the Author:	15-Aug-2017
Complete List of Authors:	Eriksson, Helena; Institute of Medicine Sahlgrenska university hospital, Occupational and environmental medicine; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Section of Occupational and Environmental Medicine Andersson, Eva; Goteborgs Universitet, 4. Occupational and Environmental Medicine, Institute of Medicine, The Sahlgrenska Academy Schiöler, Linus; Medicine, Occupational and environmental medicine Söderberg, Mia; Medicine, Occupational and environmental medicine Sjöström, Mattias; Karolinska Institutet, Institute of Environmental Medicine Rosengren, Annika; Sahlgrenska University HospitalOstra Torén, Kjell; Medicine,
Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, Coronary heart disease < CARDIOLOGY, EPIDEMIOLOGY

A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men.

Helena Eriksson[1], Eva Andersson[1], Linus Schiöler[2], Mia Söderberg[2], Sjöström M[3, 4], Annika Rosengren[5], Kjell Torén[1, 2]

1. Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden.
2. Section of Occupational and Environmental Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden.
3. Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.
4. Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.
5. Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden.

6. Corresponding author: Helena Eriksson, Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Box 414, S-405 30 Gothenburg, Sweden.
   E-mail: helena.eriksson@amm.gu.se

Word count: 2328

Abstract

Objectives: The aim was to investigate whether occupational noise increased the risk for coronary heart disease and stroke and to elucidate interactions with stressful working conditions in a cohort of Swedish men.

Design: Prospective cohort study of Swedish men followed until death, hospital discharge or until 75 years of age regarding coronary heart disease (CHD) and stroke, using Swedish national registers on cause of death and hospital discharges. Baseline data on occupation from 1974-77, was used for classification of levels of occupational noise and job demand-control. Cox regression was used to analyse the hazard ratios, HR, for CHD and stroke.

Setting: Swedish men born 1915-1925

Primary and secondary outcome measures: Coronary heart disease and stroke

Participants: Men from the primary prevention study, a random sample of 10 000 men born 1915-1925 in Gothenburg. Subjects with coronary heart disease or stroke at baseline or not employed were excluded. The remaining subjects with complete baseline data on occupation, weight, height, hypertension, diabetes, serum cholesterol and smoking constituted the study sample, 5753 men.

Results

There was an increased risk for CHD in relation to noise levels 75-85 dB(A) and >85 dB(A) compared to <75 dB(A), HR 1.15 (95% CI 1.01-1.31) and HR 1.27 (95% CI 0.99-1.63), respectively. Exposure to noise peaks also increased the risk for CHD (HR 1.19, 95% CI 1.03-1.38). Among those with high strain (high demands and low control), the risk for CHD further increased; 75-85 dB(A), 1.84 (95% CI 1.21-2.79) and >85 dB(A), 1.38 (95% CI 0.57-3.32). There was no significantly increased risk for stroke in any noise category.

Conclusions

Exposure to occupational noise was associated with an increased risk for CHD and the risk further increased among those with concomitant exposure for high strain. None of the analysed variables were related to increased risk for stroke.

Keywords: Noise, strain, CVD

Strenghts and limitations of this study

Longitudinal study with long-term follow up.

Data from national mortality register and hospital discharge register with high coverage

No individual measurements of noise

Introduction

Exposure to noise is common in many workplaces, and health effects, especially hearing disorders have been investigated since decades. In addition to the hearing effects, there are studies indicating that occupational exposure to noise may increase the risk for cardiovascular diseases, such as hypertension, coronary heart disease and stroke (1,2). The evidence is, however, rather weak, especially regarding the association with stroke where there is a conspicuous lack of prospective studies (3).

Regarding coronary heart disease and occupational exposure to noise the few available longitudinal studies seem to favour an association. In a Canadian study of 30 000 lumber mill workers there was an increased risk of acute myocardial infarction both in relation to duration of employment and in relation to noise levels (4). The highest risk was found among those who were currently working and had been employed 20 years or more with relative risks between 2.0 and 4.0. The strengths of the study were that exposure was not self-reported but based on measurements and a job exposure matrix and the outcome was based on mortality registers. One disadvantage was the lack of information on smoking habits. A 18-year follow-up of 6005 men from the Helsinki Heart Study showed an increased risk, 1.48 (95% CI 1.28-1.71) of coronary heart disease in relation to continuous noise exposure exceeding 85 dB (5). Exposure to impulse noise showed similar risk estimates. The advantages of this study are objective noise assessments, register-based outcome and access to individual data on smoking, BMI and blood pressure. In a case-control study from Sweden, subjects with myocardial infarction and controls were classified using a job-exposure matrix for occupational noise (6). There was an increased odds ratio, for occupational noise exceeding 75 dBA, but with adjustments for age, sex, smoking, socioeconomic status and air pollution the risk decreased and became insignificant.

There is conflicting evidence whether occupational exposure to noise increases the risk for stroke (3). A source of confusion is that stroke comprises different subtypes such as ischemic stroke, intra-cerebral bleeding and sometimes also sub-arachnoidal bleeding is included in the stroke concept. In some studies, stroke is included in the broader concept of cardiovascular diseases. As all those clinical subtypes of stroke may have different risk factors, there may be considerable misclassification in the stroke epidemiological studies. We have identified only two longitudinal studies albeit showing contradictory results (7,8). A Japanese study comprising 14568 subjects from the general population with self-reported noise levels from their workplaces. They were followed for approximately 15 years, and the outcome (mortality) was based on population registries. In adjusted models the hazard ratio for intra-cerebral bleeding was 2.1 (1.01-4.4). The hazard ratio for ischemic stroke was 1.7 (0.7-4.1). In the Danish study more than 200000 workers were followed for six years and the outcome, stroke morbidity, was identified by national in-patient registries (8). The baseline exposure to occupational noise was assigned to each worker according to company, calendar year and occupation. The assigned noise levels were obtained from measurements on 1077 workers in 168 companies. The study did not show any increased risk of stroke in relation to occupational noise exposure.

Exposure to work-place related stress is often classified according to the job-demand-control model (9), through the literature high strain, the combination of high demands and low control, has been linked to ill-health primarily coronary heart disease (10). A recent meta-analysis of 13 studies concluded that the association to coronary heart disease was rather modest, hazard ratio 1.23 (11). However, there seems to be interactions between job-strain and life-style factors like smoking, being obese or reporting low physical activity (12). Interactions have been reported between occupational noise and psychological demands or decision latitude as well as interaction between noise exposure and smoking (6,13).

The aim of the present study was to investigate whether occupational exposure to noise increased the risk for coronary heart disease and stroke, and to elucidate potential interactions with stressful psychosocial work conditions based on the job-demand-control model in a longitudinal general population study.

Methods

Study population

The Primary Prevention Study (PPS) is a cohort study obtained from a general-population sample as previously described (14,15). The source population comprised 10 000 men, a random third of all men living in Gothenburg born between 1915 and 1925, of whom 7494 participated in screening examinations between January 1970 and March 1973. Three years later, 1974-1977, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we used the follow-up data as our baseline since it includes occupational data and information about age, body mass index (BMI), BMI is the weight in kilograms divided by the square of the body height in meters, serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, physician diagnosed diabetes (yes/no), physician diagnosed hypertension (yes/no), coronary heart disease (yes/no) or stroke (yes/no) and smoking as previously described (16).

Subjects with coronary heart disease or stroke at baseline (n=329) and subjects not employed (n=730) were excluded, leaving 6074. The remaining subjects with complete baseline data on occupation, weight, height, hypertension, diabetes, serum cholesterol and smoking constituted the study sample, (n=5753) (Table 1). All participants gave their informed consent to participate in the study and it was approved by the Regional Ethical Review Board, Gothenburg University, Sweden.

Table 1. Baseline characteristics of 5753 Swedish men in a general population study, by different noise exposure levels.

	Low exposure <75 dB(A) n=2930	Medium exposure 75-85dB(A) n=2467	High exposure >85dB(A) n=356	Low probability of noise peaks n=3718	High probability of noise peaks n=1278	Overall n=5753
Mean age, yrs (SD)	55.2 (2.1)	55.3 (2.0)	55.3 (2.0)	55.3 (2.1)	55.3 (2.0)	55.3 (2.1)
Mean cholesterol, mmol/L (SD)	6.4 (1.04)	6.4 (1.04)	6.4 (1.12)	6.4 (1.04)	6.4 (1.04)	6.4 (1.05)
Mean SBP, mm Hg (SD)	145.3 (19.6)	146.3 (19.6)	146.1 (19.6)	145.7(19.6)	146.4(19.8)	145.8 (19.6)
Mean BMI, kg/m^2 (SD)	25.4 (3.1)	25.8 (3.3)	25.8 (3.0)	25.5 (3.2)	25.9 (3.3)	25.6 (3.2)
BMI <18.5, % (n)	0.5% (n=15)	0.3% (n=8)	0.3% (n=1)	0.5% (n=18)	0.3% (n=4)	0.4% (n=24)
BMI 18.5-<25, % (n)	47.0% (n=1376)	43.0% (n=1061)	40.2% (n=143)	46.1% (n=1712)	40.9% (n=522)	44.9% (n=2580)
BMI 25-<30, % (n)	45.3% (n=1328)	47.1% (n=1163)	50.0% (n=178)	45.4% (n=1687)	49.8% (n=637)	46.4% (n=2669)
BMI >=30 %, (n)	7.2% (n=211)	9.5% (n=235)	9.6% (n=34)	8.1% (n=301)	9.0% (n=115)	8.3% (n=480)
Diabetes, % (n)	2.7% (n=80)	2.9% (n=71)	3.4% (n=12)	2.8% (n=105)	2.6% (n=33)	2.8%(n=163)
Hypertension, % (n)	21.5% (n=629)	22.3% (n=551)	21.6% (n=77)	21.7% (n=808)	23.3% (n=298)	21.8% (n=1257)
Ever smoker, % (n)	73.3% (n=2148)	76.8% (n=1894)	77.8% (n=277)	74.3% (n=2763)	78.6%(n=1005)	75.1% (n=4319)
High strain, % (n)	7.3% (n=215)	16.7% (n=413)	9.6% (n=34)	13.8% (n=512)	4.6% (n=59)	11.5%(n=662)

The category maybe noise peaks n=757 are not included in noise peak analysis. BMI is the weight in kilograms divided by the square of the body height in meters.

For assessing occupational noise exposure, a previously developed job-exposure matrix (JEM) was applied (17). The JEM is based on 145 measurement reports and a total of 569 measurements on 129 unique job families. It classifies 321 occupations based on the NYK - 85/90 according to noise levels and peak levels. The JEM classification is covering the period from 1970 to 2004 in five-year intervals.

The noise levels were categorized into three different levels, low; <75 dB(A), medium; 75-85 dB(A) and high; > 85 dB(A) in the JEM. There was also an assessment of whether there was a high risk of peak level noise exposure and the categories 'Yes, for sure' and 'Yes, probably' was compared with the category 'Unlikely'. The category 'Yes, maybe' (n=757 and 135 cases) were not included in the noise peak analyses.

For assessing the psychosocial workplace exposure, we used a previously published and used job-exposure matrix (18,19). The JEM provides separate estimates of job demand and control for 261 occupations separated into gender and age (25 to 44 and 45 to 74) as previously described (16,20). Job demands and decision latitude were explored with four items each in the JEM, and all subjects were assigned a certain score based on occupation and age. Using the median of the distribution as cut-off, which is standard procedure, demand and control were dichotomized as high or low. The participants were then allocated into four categories; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

Based on Sweden's unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.

All discharges from Gothenburg hospitals have been entered into the national register since 1970, with the exception of 1976. The outcomes were classified according to ICD-8 code until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Coronary heart disease was defined as 410-414 (ICD8, 9) and as I20-I25 (ICD 10) from the death register and as acute myocardial infarction 410 and I21 from the discharge register, respectively. Stroke events, including both ischemic stroke and intracerebral bleeding, were defined as death or hospitalisation with ICD codes 431-438 (ICD8, 9) and I61-I69 (ICD 10). Each type of event was treated separately and only the first event of each type was used in the analysis.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material was analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (21) using the R package Survival. Proportional hazards assumptions were found reasonable except for the analysis of smoking and serum cholesterol which we stratified for in the risk factor adjusted models. Hospital care or mortality (whatever came first) from coronary heart disease or stroke were considered events and time were measured as months since baseline. The observation period stopped at the age of 75. Analyses

were also performed restricted to subjects younger than 65 years. In the crude models hazard ratios (HR) and 95% confidence intervals (CI) were calculated using the occupational noise exposure and age as explanatory variables. Tests for trend were performed by including the covariate as a continuous variable.

In the risk factor adjusted models we adjusted for ever-smoking (yes/no), cholesterol (quartiles), history of diabetes (yes/no), hypertension (yes/no), and BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25). Interaction between occupational noise exposure and high strain was analysed separately, the population was divided in two groups, subjects exposed for high strain versus others not exposed for high strain and hazard ratios were calculated.

Results

During the follow-up period of totally 94222 person-years (mean years per person 16,4) there were 1004 events of coronary heart disease (Table 2). The Cox regression models adjusted for age showed an increased hazard ratio (HR) for coronary heart disease in relation to medium levels (HR 1.15, 95% CI 1.01-1.31) and high levels (HR 1.27, 95% CI 0.99-1.63) of occupational noise exposure (Table 2) and a positive trend.

Table 2. Incidence and Hazard Ratios (HR) with confidence intervals (CI) for coronary heart disease and stroke in relation to exposure for occupational noise among all men (n=5753).

	Events per 1000 observation years (n cases)	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)
Coronary heart disease, all	10.7 (n=1004)		
Low noise, <75 dB(A)	9.8 (n=480)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	11.4 (n=453)	1.15 (1.01-1.31)	1.13 (0.99-1.28)
High noise, >85 dB(A)	12.4 (n=71)	1.27 (0.99-1.63)	1.22 (0.95-1.56)
p for trend		0.01	0.03
Noise peaks unlikely	10.2 (n=622)	1.00 (ref)	1.00 (ref)
Noise peaks likely	12.1 (n=247)	1.19 (1.03-1.38)	1.16 (1.00-1.34)
Coronary heart disease, subjects ≤65 years	7.5 (n=375)		
Low noise, <75 dB(A)	6.7 (n=174)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	8.2 (n=172)	1.20 (0.97-1.48)	1.17 (0.94-1.44)
High noise, >85 dB(A)	9.4 (n=29)	1.38 (0.93-2.05)	1.30 (0.88-1.93)
p for trend		0.04	0.09
Noise peaks unlikely	7.5 (n=243)	1.00 (ref)	1.00 (ref)
Noise peaks likely	8.3 (n=91)	1.11 (0.87-1.41)	1.07 (0.84-1.36)

	Events per 1000 observation years (n cases)	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)
Stroke, all	5.4 (n=517)		
Low noise, <75 dB(A)	5.3 (n=262)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	5.4 (n=220)	1.02 (0.85-1.22)	1.00 (0.84-1.21)
High noise, >85 dB(A)	6.0 (n=35)	1.16 (0.82-1.65)	1.12 (0.79-1.59)
p for trend		p=0.51	p=0.65
Noise peaks unlikely	5.4 (n=336)	1.00 (ref)	1.00 (ref)
Noise peaks likely	5.8 (n=122)	1.08 (0.88-1.33)	1.06 (0.86-1.30)
Stroke, subjects ≤65 years	2.7 (n=138)		
Low noise, <75 dB(A)	2.8 (n=73)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	2.5 (n=54)	0.89 (0.63-1.27)	0.90 (0.63-1.28)
High noise, >85 dB(A)	3.5 (n=11)	1.26 (0.67-2.37)	1.23 (0.65-2.32)
p for trend		p=0.97	p=0.98
Noise peaks unlikely	2.7 (n=89)	1.00 (ref)	1.00 (ref)
Noise peaks likely	3.3 (n=37)	1.23 (0.84-1.81)	1.23 (0.83-1.80)

*age in years, baseline BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25), baseline diabetes, hypertension and by stratification never/ever smoker, cholesterol in quartiles

Exposure to noise peaks also increased the risk for coronary heart disease (HR 1.19, 95% CI 1.03-1.38). In the risk factor adjusted models all estimates were slightly diminished but regarding noise peaks the statistical significance remained. When the risk for coronary heart disease was restricted to subjects younger than 65 years, the risk estimates increased, but due to lack of power the confidence intervals turned wider and included unity.

For the follow-up period there were 517 stroke events. There was no increased risk for stroke in any of the exposure strata, medium levels, high levels or peaks of noise exposure (Table 2).

In Table 3, risk estimates for occupational noise exposure are outlined in the different groups of high strain and not high strain. Among those who were classified as having high strain and medium occupational noise exposure, the risk for coronary heart disease further increased (HR 1.73, 95% CI 1.14-2.64), risk factor adjusted. Among those with high occupational noise exposure the risk also increased (HR 1.62, 95% CI 0.67-3.90), but the confidence interval was wide and included unity. The interaction analyses regarding stroke were negative.

Table 3. Interaction between occupational noise exposure and high strain. Hazard ratios (HR) with confidence intervals for coronary heart disease and stroke in subjects exposed for high strain versus not exposed for high strain in relation to exposure for occupational noise among all men (n=5753).

	Age adjusted HR (95% CI)		Risk factor adjusted* HR (95% CI)	
	High strain	**Not high strain**	**High strain**	**Not high strain**
Coronary heart disease n=1004 events				
Low noise, <75 dB(A)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	1.84 (1.21-2.79)	1.07 (0.93-1.23)	1.73 (1.14-2.64)	1.06 (0.92-1.22)
High noise, >85 dB(A)	1.38 (0.57-3.32)	1.27 (0.98-1.65)	1.62 (0.67-3.90)	1.19 (0.92-1.55)
Noise peaks unlikely	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Noise peaks likely	1.25 (0.70-2.23)	1.20 (1.09-1.40)	1.29 (0.72-2.31)	1.16 (0.99-1.35)
Stroke n=517 events				
Low noise, <75 dB(A)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	1.37 (0.78-2.42)	0.98 (0.81-1.18)	1.41 (0.80-2.49)	0.97 (0.80-1.17)
High noise, >85 dB(A)	0.82 (0.20-3.55)	1.19 (0.83-1.72)	0.97 (0.22-4.20)	1.13 (0.79-1.63)
Noise peaks unlikely	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Noise peaks likely	1.44 (0.65-3.19)	1.07 (0.87-1.33)	1.34 (0.61-2.81)	1.04 (0.84-1.30)

*age in years, baseline BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25), baseline diabetes, hypertension and by stratification never/ever smoker, cholesterol in quartiles

Discussion

The present study shows an increased risk for coronary heart disease in relation to both continuous noise and peaks of occupational exposure to noise. Concomitant exposure for high strain further increased the risk of CHD. There was no increased risk for stroke in relation to occupational noise exposure.

This study has several advantages such as high external validity because a general-population sample with a long period of follow-up was available and near complete follow up. The use of a national mortality register and hospital discharge register with high coverage further increase the validity of the results. However, there are also several limitations. Regarding the stroke outcome, the restricted number of cases and lack of computerized tomography during early follow up did not allow for analyses of subtypes of stroke. Second, there were no individual measurements of the noise levels for the participants; instead the assigned exposure

was estimated from average levels in similar work places. However, the assessment of noise exposure and job-strain based on job exposure matrices, may display less bias than self-reports. But there may be a considerable non-differential misclassification of the exposure estimates causing attenuating of the risk estimates. Of importance is also that the study comprises only men which limit its external validity. We had access to individual baseline data regarding smoking habits, BMI, diabetes, hypertension, and cholesterol; this made it possible to have a careful control of interactions and confounding. In general, we have simple, only age adjusted models as risk factors can be mediators, but we also present risk factor adjusted models. We adjusted for diabetes, which have been disputed as diabetes may be part of the causal chain from noise to coronary heart disease (6). Adding diabetes to our model did, however, not affect our risk estimates. We did not adjust for socioeconomic status as it could implicate an over-adjustment; the exposure is based on occupations, which usually comprise the socioeconomic position.

We used the job held at the age of 50 years, which probably in most cases reflects the longest held job. We also analysed the risk below 65 years and found higher risks in working age. This may reflect that the risk of coronary heart disease is dependent on current noise exposure and that the risk may decrease after termination of the work as observed by others (4,13).

Our results regarding coronary heart disease corroborate earlier studies, giving further evidence for a causal relation between occupational noise exposure and increased risk for coronary heart disease (5,6). We also support the findings by Selander et al that high strain (high demand/low control) further increased the risk for coronary heart disease (6). The results from the present study indicate that exposure to occupational noise is not increasing the risk for stroke, and there was no interaction with job strain. This could be due to power, suboptimal classification of the different subtypes of stroke or perhaps that stroke has a different pattern of occupational risk factors compared to coronary heart disease.

Conclusions

Exposure to occupational noise increased the risk for coronary heart disease. There was no increased risk for stroke in any of the noise exposure categories. There were indications of an interaction between noise exposure and work-related strain, and further studies are needed to elucidate patterns of interactions between different occupational risk factors.

References

1. Skogstad M, Johannessen HA, Tynes T et al. Systematic review of the cardiovascular effects of occupational noise. *Occup Med* 2016;66:10-16.
2. Theorell T, Jood K, Järvholm LS et al. A systematic review of studies in the contributions of the work environment to ischaemic heart disease development. *Eur J Public Health* 2016;26:470–77.
3. Kolstad HA, Stokholm Z, Hansen ÅM et al. Whether noise exposure causes stroke or hypertension is still not known. *BMJ* Online [eLetter] 16 December 2013. http://www.bmj.com/content/347/bmj.f7444.long
4. Davies HW, Teschke K, Kenedy SM et al. Occupational exposure to noise and mortality from acute myocardial infarction. *Epidemiology* 2005;16:25-32.
5. Virkkunen H, Kauppinen T, Tenkanen L. Long-term effect of occupational noise on the risk of coronary heart disease. *Scand J Work Environ Health* 2005;31:291-299.
6. Selander J, Bluhm G, Nilsson M et al. Joint effects of job strain and road-traffic and occupational noise on myocardial infarction. *Scand J Work Env Health* 2013;39:195-203.
7. Fujino Y, Iso H, Tamakoshi A, for the JACC study group. A prospective cohort study of perceived noise exposure at work and cerebrovascular diseases among male workers in Japan. *J Occup Health* 2007;49:382-388.
8. Stokholm ZA, Bonde JP, Christensen KL et al. Occupational noise exposure and the risk of stroke. *Stroke* 2013;44:3214-3216.
9. Karasek RA. Job demands, job decision latitude, and mental strain: Implications for job redesign. *Admin Sci Qtrly* 1979;24:285-308.
10. Eller NH, Netterstrøm B, Gyntelberg F et al. Work-related psychosocial factors and the development of ischemic heart disease: a systematic review. *Cardiol Rev* 2009;17:83-97.
11. Kivimäki M, Nyberg ST, Batty GD et al. Job strain as a risk factor for coronary heart disease: A collaborative meta-analysis of individual participant data. *Lancet* 2012;380:1491-1497.
12. Kivimäki M, Nyberg ST, Fransson EI et al. Associations of job strain and lifestyle factors with risk of coronary artery disease: A meta-analysis of individual participant data. *Can Med Assoc J* 2013;185:763-769.
13. Gan WQ, Davies HW, Demers PA. Exposure to occupational noise and cardiovascular disease in the United States: the National Health and Nutrition Examination Survey 1999-2004. *Occup Env Med* 2011;68:183-190.
14. Wilhelmsen L, Berglund G, Elmfeldt D et al. The multifactor primary prevention trial in Goteborg, Sweden. *Eur Heart J* 1986;7:279-288.
15. Harmsen P, Lappas G, Rosengren A et al. Long-term risk factors for stroke: Twenty-eight years of follow-up of 7457 middle-aged men in Göteborg, Sweden. *Stroke* 2006; 37:1663-1667.
16. Torén K, Schiöler L, Söderberg M et al. The association between job strain and atrial fibrillation in Swedish men. *Occup Environ Med* 2015;72:177-180.
17. Sjöström M, Lewné M, Alderling M et al. A job-exposure matrix for occupational noise: Development and validation. *Ann Occup Hyg* 2013;57:774-783.

18. Johnson JV, Stewart W, Hall EM et al. Long-term psychosocial work environment and cardiovascular mortality among Swedish men. *Am J Public health* 1996;86:324-331.
19. Fredlund P, Hallqvist J, Diderichsen F. Psykosocial yrkesexponeringsmatris. *Arbete och Hälsa* 2000;11:1-37 [In Swedish].
20. Torén K, Schiöler L, Giang WK et al. A longitudinal general population-based study of job strain and risk for coronary heart disease and stroke in Swedish men. *BMJOpen* 2014;4:e004355
21. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika* 1994;81:515-526.

Footnotes

- **Contributors**: Rosengren, Torén, Andersson conceptualized, designed and supervised the study. Eriksson helped to conceive the study and drafted the manuscript. Sjöström has participated in developing the job exposure matrix regarding noise. Schiöler performed the statistical analyses. Söderberg critically revised the manuscript. All authors were responsible for the drafting of the manuscript and for the final approval of the manuscript.

- **Funding**: The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation.

- **Competing interests**: None. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: *no support from any organisation for the submitted work*; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work

- **Ethics statement**: Ethics approval by the Ethics Committee for Medical Research at the University of Gothenburg.

- **Provenance and peer review**: Not commissioned; externally peer reviewed.

- **Data sharing statement**: This is a large general population study which has been followed for many years. There are unpublished data in the dataset. Scientific cooperation around this study is possible.

STROBE. **A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men.** 2017-08-14. Helena Eriksson.

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract YES
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found YES
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported YES
Objectives	3	State specific objectives, including any prespecified hypotheses YES
Methods		
Study design	4	Present key elements of study design early in the paper YES
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection YES
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. YES *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. YES
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. YES
Bias	9	Describe any efforts to address potential sources of bias. YES
Study size	10	Explain how the study size was arrived at. YES
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. YES
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding. YES
		(*b*) Describe any methods used to examine subgroups and interactions. YES
		(*c*) Explain how missing data were addressed. YES
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed. YES *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. YES
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. YES
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount). YES
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time YES
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. YES
		(*b*) Report category boundaries when continuous variables were categorized. YES
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses. YES
Discussion		
Key results	18	Summarise key results with reference to study objectives. YES
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. YES
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. YES
Generalisability	21	Discuss the generalisability (external validity) of the study results. YES
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. YES

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019160.R1
Article Type:	Research
Date Submitted by the Author:	11-Dec-2017
Complete List of Authors:	Eriksson, Helena; Institute of Medicine Sahlgrenska university hospital, Occupational and environmental medicine; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Section of Occupational and Environmental Medicine Andersson, Eva; Goteborgs Universitet, 4. Occupational and Environmental Medicine, Institute of Medicine, The Sahlgrenska Academy Schiöler, Linus; Medicine, Occupational and environmental medicine Söderberg, Mia; Medicine, Occupational and environmental medicine Sjöström, Mattias; Karolinska Institutet, Institute of Environmental Medicine Rosengren, Annika; Sahlgrenska University HospitalOstra Torén, Kjell; Medicine,
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, Coronary heart disease < CARDIOLOGY, EPIDEMIOLOGY

A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men.

Helena Eriksson[1], Eva Andersson[1], Linus Schiöler[2], Mia Söderberg[2], Mattias Sjöström[3, 4], Annika Rosengren[5], Kjell Torén[1, 2]

1. Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden.
2. Section of Occupational and Environmental Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden.
3. Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.
4. Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.
5. Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden.

Corresponding author: Helena Eriksson, Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Box 414, S-405 30 Gothenburg, Sweden.
E-mail: helena.eriksson@amm.gu.se

Word count: abstract 295, main text 2628.

Abstract

Objectives: The aim was to investigate whether occupational noise increased the risk for coronary heart disease and stroke and to elucidate interactions with stressful working conditions in a cohort of Swedish men.

Design: Prospective cohort study of Swedish men followed until death, hospital discharge or until 75 years of age regarding coronary heart disease (CHD) and stroke, using Swedish national registers on cause of death and hospital discharges. Baseline data on occupation from 1974-77, was used for classification of levels of occupational noise and job demand-control. Cox regression was used to analyse the hazard ratios, HR, for CHD and stroke.

Setting: Swedish men born 1915-1925

Primary and secondary outcome measures: Coronary heart disease and stroke

Participants: Men from the Primary Prevention Study, a random sample of 10 000 men born 1915-1925 in Gothenburg. Subjects with coronary heart disease or stroke at baseline or not employed were excluded. The remaining subjects with complete baseline data on occupation, weight, height, hypertension, diabetes, serum cholesterol and smoking constituted the study sample, 5753 men.

Results

There was an increased risk for CHD in relation to noise levels 75-85 dB(A) and >85 dB(A) compared to <75 dB(A), HR 1.15 (95% CI 1.01-1.31) and HR 1.27 (95% CI 0.99-1.63), respectively. Exposure to noise peaks also increased the risk for CHD (HR 1.19, 95% CI 1.03-1.38). Among those with high strain (high demands and low control) combined with noise >75 dB(A), the risk for CHD further increased; HR 1.80 (95% CI 1.19-2.73). There was no significantly increased risk for stroke in any noise category.

Conclusions

Exposure to occupational noise was associated with an increased risk for CHD and the risk further increased among those with concomitant exposure for high strain. None of the analysed variables were related to increased risk for stroke.

Keywords: Noise, strain, IHD, CVD

Strenghts and limitations of this study

Longitudinal study with long-term follow up.

Data from national mortality register and hospital discharge register with high coverage

No individual measurements of noise

Introduction

Cardiovascular diseases are common diseases in Sweden as in most countries, in 2016, 25700 persons suffered from acute myocardial infarction and 25% of these died within 28 days (1) and the same year 26500 suffered from a stroke and of these, 26% died within 28 days (2).

Exposure to noise is frequent in many workplaces, and health effects, especially hearing disorders have been investigated since decades (3). In addition to the hearing effects, there are studies indicating that occupational exposure to noise may increase the risk for cardiovascular diseases, such as hypertension, coronary heart disease and stroke (4-8). The evidence is, however, rather weak, especially regarding the association with stroke where there is a conspicuous lack of prospective studies (9). Regarding coronary heart disease and occupational exposure to noise, the few available longitudinal studies seem to favour an association. In a Canadian study of 30 000 lumber mill workers there was an increased risk of fatal acute myocardial infarction both in relation to duration of employment and in relation to noise levels (10). A Finnish study showed an increased risk for coronary heart disease in relation to continuous noise exposure exceeding 85 dB(A), impulse noise also showed an increased risk (11).

There are few studies and there is conflicting evidence whether occupational exposure to noise increases the risk for stroke (9). A Japanese study (12) showed an increased hazard ratio for intra-cerebral bleeding but not for ischemic stroke. A Danish study (13) of more than 200000 workers did not show an increased risk of stroke in relation to occupational noise exposure. In an Australian study of 2942 subjects there was a significant association between the incidence of stroke and those exposed to very high levels of noise (14).

In a study from 2016 based on noise exposure and occurrence of stroke in the US general population there was no statistically significant association between exposure for noise and stroke after adjustment for sociodemographics, lifestyle and comorbidity (15).

The mechanisms regarding occupational noise exposure and risk for cardiovascular disease are not clear. Environmental noise and the mechanisms behind the increased risk for cardiovascular disease has been studied to a larger extent (16). Noise exposure activates the autonomic and endocrine systems, the blood pressure increases, the heart rate is altered and stress hormones are released. Chronic noise exposure can affect blood pressure, blood glucose, blood lipids and viscosity leading to an increased risk for cardiovascular disease (16).

Exposure to work-place stress is often evaluated according to the job-demand-control model (17). Throughout the literature, high strain, the combination of high demands and low control, has been linked to ill-health primarily coronary heart disease (18). A recent meta-analysis of 13 studies concluded that the association to coronary heart disease was rather small but consistent, hazard ratio 1.23 (19). However, there seems to be interactions between job-strain and occupational noise (20).

The aim of the present study was to investigate whether occupational exposure to noise increased the risk for coronary heart disease and stroke, and to elucidate potential interactions with stressful psychosocial work conditions based on the job-demand-control model in a longitudinal general population study.

Methods

Study population

The Primary Prevention Study (PPS) is a cohort study obtained from a general-population sample as previously described (21,22*).* The source population comprised 10 000 men, a random third of all men living in Gothenburg born between 1915 and 1925, of whom 7494 participated in screening examinations between January 1970 and March 1973. Three years later, 1974-1977, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we used the follow-up data as our baseline since it includes occupational data and information about age, body mass index BMI, (BMI is the weight in kilograms divided by the square of the body height in meters), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, physician diagnosed diabetes (yes/no), physician diagnosed hypertension (yes/no), coronary heart disease (yes/no) or stroke (yes/no) and smoking as previously described (23).

Subjects with coronary heart disease or stroke at baseline (n=329) and subjects not employed (n=730) were excluded, leaving 6074. The remaining subjects with complete baseline data on occupation, weight, height, hypertension, diabetes, serum cholesterol and smoking constituted the study sample, (n=5753) with an age range of 50-59 years (Table 1). All participants gave their informed consent to participate in the study and it was approved by the Regional Ethical Review Board, Gothenburg University, Sweden.

Table 1. Baseline characteristics of 5753 Swedish men in a general population study, by different noise exposure levels.

	Low exposure <75 dB(A) n=2930	Medium exposure 75-85dB(A) n=2467	High exposure >85dB(A) n=356	Noise peaks unlikely n=3718	Noise peaks maybe n=757	Noise peaks likely n=1278	Overall n=5753
Mean age, yrs (SD)	55.2 (2.1)	55.3 (2.0)	55.3 (2.0)	55.3 (2.1)	55.2 (2.0)	55.3 (2.0)	55.3 (2.1)
Mean cholesterol, mmol/L (SD)	6.4 (1.04)	6.4 (1.04)	6.4 (1.12)	6.4 (1.04)	6.4 (1.09)	6.4 (1.04)	6.4 (1.05)
Mean SBP, mm Hg (SD)	145.3 (19.6)	146.3 (19.6)	146.1 (19.6)	145.7 (19.6)	145.4 (19.1)	146.4 (19.8)	145.8 (19.6)
Mean BMI, kg/m^2 (SD)	25.4 (3.1)	25.8 (3.3)	25.8 (3.0)	25.5 (3.2)	25.5 (3.1)	25.9 (3.3)	25.6 (3.2)
BMI <18.5, % (n)	0.5% (n=15)	0.3% (n=8)	0.3% (n=1)	0.5% (n=18)	0.3% (n=2)	0.3% (n=4)	0.4% (n=24)
BMI 18.5-<25, % (n)	47.0% (n=1376)	43.0% (n=1061)	40.2% (n=143)	46.1% (n=1712)	45.7% (n=346)	40.9% (n=522)	44.9% (n=2580)
BMI 25-<30, % (n)	45.3% (n=1328)	47.1% (n=1163)	50.0% (n=178)	45.4% (n=1687)	45.6% (n=345)	49.8% (n=637)	46.4% (n=2669)
BMI >=30 %, (n)	7.2% (n=211)	9.5% (n=235)	9.6% (n=34)	8.1% (n=301)	8.5% (n=64)	9.0% (n=115)	8.3% (n=480)
Diabetes, % (n)	2.7% (n=80)	2.9% (n=71)	3.4% (n=12)	2.8% (n=105)	3.3% (n=25)	2.6% (n=33)	2.8%(n=163)
Hypertension, % (n)	21.5% (n=629)	22.3% (n=551)	21.6% (n=77)	21.7% (n=808)	19.9% (n=151)	23.3% (n=298)	21.8% (n=1257)
Ever smoker, % (n)	73.3% (n=2148)	76.8% (n=1894)	77.8% (n=277)	74.3% (n=2763)	72.8% (n=551)	78.6%(n=1005)	75.1% (n=4319)
High strain, % (n)	7.3% (n=215)	16.7% (n=413)	9.6% (n=34)	13.8% (n=512)	12.0% (n=91)	4.6% (n=59)	11.5% (n=662)

BMI is the weight in kilograms divided by the square of the body height in meters.

For assessing occupational noise exposure, a previously developed job-exposure matrix (JEM) regarding noise was applied (24). The noise JEM is based on 145 measurement reports and a total of 569 measurements on 129 unique job families. It classifies 321 occupations based on the NYK -85/90 according to noise levels and peak levels. The noise JEM classification is covering the period from 1970 to 2004 in five-year intervals.

The noise levels were categorized into three different levels, low; <75 dB(A), medium; 75-85 dB(A) and high; > 85 dB(A) in the JEM. There was also an assessment of whether there was a high risk of peak level noise exposure and the categories: 'Noise peaks likely' ('Yes, for sure' combined with 'Yes, probably') and 'Noise peaks maybe' was compared with the category 'Noise peaks unlikely'.

For assessing the psychosocial workplace exposure, we used a previously published and used job-exposure matrix (25, 26). This psychosocial JEM provides separate estimates of job demand and control for 261 occupations separated into gender and age (25 to 44 and 45 to 74) as previously described (23, 27). Job demands and decision latitude were explored with four items each, and all subjects were assigned a certain score based on occupation and age in this psychosocial JEM. Using the median of the distribution as cut-off, which is standard procedure, demand and control were dichotomized as high or low. The participants were then allocated into four categories; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

Based on Sweden's unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.

All discharges from Gothenburg hospitals have been entered into the national register since 1970, with the exception of 1976. The outcomes were classified according to ICD-8 code until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Coronary heart disease was defined as 410-414 (ICD-8, 9) and as I20-I25 (ICD-10) from the death register and as acute myocardial infarction 410 and I21 from the discharge register, respectively. Stroke events, including both ischemic stroke and intracerebral bleeding, were defined as death or hospitalisation with ICD codes 431-438 (ICD-8, 9) and I61-I69 (ICD-10). Each type of event was treated separately and only the first event of each type was used in the analysis.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material was analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (28) using the R package Survival. Proportional hazards assumptions were found reasonable except for the analysis of smoking and serum cholesterol which we stratified for in the risk factor adjusted models. Hospital care or mortality (whatever came first) from coronary heart disease or stroke were considered events and time were measured as months since baseline. The observation period stopped at the age of 75. Analyses were also performed restricted to subjects younger than 65 years. In the crude models hazard ratios (HR) and 95% confidence intervals (CI) were calculated using the occupational noise exposure and age as explanatory variables. Tests for trend were performed by including the covariate as a continuous variable.

In the risk factor adjusted models we adjusted for ever-smoking (yes/no), cholesterol (quartiles), history of diabetes (yes/no), hypertension (yes/no), and BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25). Interaction between occupational noise exposure and high strain was analysed separately, here the noise exposure was aggregated into <75 and >75 dB(A) to gain power. The population was divided in two groups, subjects exposed for high strain versus others not exposed for high strain and hazard ratios were calculated. Wald test was used to test interaction.

A sensitivity analysis was performed restricted to the subjects without hypertension and diabetes, potentially mediators for coronary heart disease.

Results

During the follow-up period of totally 94222 person-years (mean years per person 16.4) there were 1004 events of coronary heart disease (Table 2). The Cox regression models adjusted for age showed an increased hazard ratio for coronary heart disease in relation to medium levels (HR 1.15, 95% CI 1.01-1.31) and high levels (HR 1.27, 95% CI 0.99-1.63) of occupational noise exposure (Table 2) and a positive trend.

Table 2. Incidence and Hazard Ratios (HR) with confidence intervals (CI) for coronary heart

	Events per 1000 observation years (n events)	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)
Coronary heart disease, all	10.7 (n=1004)		
Low noise, <75 dB(A)	9.8 (n=480)	1.00 (ref)	1.00 (ref)

disease and stroke in relation to exposure for occupational noise among all men (n=5753).

	Events per 1000 observation years (n events)	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)
Medium noise, 75-85 dB(A)	11.4 (n=453)	1.15 (1.01-1.31)	1.13 (0.99-1.28)
High noise, >85 dB(A)	12.4 (n=71)	1.27 (0.99-1.63)	1.22 (0.95-1.56)
p for trend		p=0.01	p=0.03
Stroke, all	5.4 (n=517)		
Low noise, <75 dB(A)	5.3 (n=262)	1.00 (ref)	1.00 (ref)
Noise peaks unlikely	10.2 (n=622)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	5.4 (n=220)	1.02 (0.85-1.22)	1.01 (0.84-1.21)
Noise peaks maybe	10.6 (n=135)	1.05 (0.87-1.26)	1.04 (0.86-1.25)
High noise, >85 dB(A)	6.0 (n=35)	1.16 (0.82-1.65)	1.12 (0.79-1.59)
Noise peaks likely	12.1 (n=247)	1.19 (1.03-1.38)	1.16 (1.00-1.34)
p for trend		p=0.51	p=0.65
p for trend		p=0.03	p=0.06
Noise peaks unlikely	5.4 (n=336)	1.00 (ref)	1.00 (ref)
Coronary heart disease, Noise peaks maybe	4.5 (n=59)	0.83 (0.63-1.10)	0.84 (0.63-1.10)
subjects ≤65 years	7.5 (n=375)		
Low noise, <75 dB(A)	6.7 (n=174)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	8.2 (n=172)	1.20 (0.97-1.48)	1.17 (0.94-1.44)
High noise, >85 dB(A)	9.4 (n=29)	1.38 (0.93-2.05)	1.30 (0.88-1.93)
p for trend		p=0.04	p=0.09
Noise peaks unlikely	7.5 (n=243)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	6.1 (n=41)	0.82 (0.58-1.13)	0.82 (0.59-1.14)
Noise peaks likely	8.3 (n=91)	1.11 (0.87-1.41)	1.07 (0.84-1.36)
p for trend		p=0.60	p=0.81

Noise peaks likely	5.8 (n=122)	1.08 (0.88-1.33)	1.06 (0.86-1.30)
p for trend		p=0.65	p=0.82
Stroke, subjects ≤65 years	2.7 (n=138)		
Low noise, <75 dB(A)	2.8 (n=73)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	2.5 (n=54)	0.89 (0.63-1.27)	0.90 (0.63-1.28)
High noise, >85 dB(A)	3.5 (n=11)	1.26 (0.67-2.37)	1.23 (0.65-2.32)
p for trend		p=0.97	p=0.98
Noise peaks unlikely	2.7 (n=89)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	1.8 (n=12)	0.65 (0.36-1.19)	0.66 (0.36-1.20)
Noise peaks likely	3.3 (n=37)	1.23 (0.84-1.81)	1.23 (0.83-1.80)
p for trend		p=0.46	p=0.47

*age in years, baseline BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25), baseline diabetes, hypertension and by stratification never/ever smoker, cholesterol in quartiles

Exposure to noise peaks also increased the risk for coronary heart disease (HR 1.19, 95% CI 1.03-1.38). In the risk factor adjusted models all estimates were slightly diminished but regarding noise peaks the statistical significance remained. When the risk for coronary heart disease was restricted to subjects younger than 65 years, the risk estimates increased, but due to lack of power the confidence intervals turned wider and included unity.

When analyzing the cohort without the subjects with hypertension and diabetes at baseline (n=4400), the HR for coronary heart disease was 1.20 (95% CI 1.03-1.41) in relation to medium level of noise exposure and HR 1.49 (95% CI 1.11-1.99) in relation to high level of noise exposure and for the subjects with likely exposure for noise peaks the HR was 1.30 (95% CI 1.09-1.55).

In the follow-up period, there were 517 stroke events. There was no increased risk for stroke in any of the exposure strata, medium levels, high levels or peaks of noise exposure (Table 2).

In Table 3, risk estimates for occupational noise exposure are outlined in the different groups of high strain and not high strain. Among those who were classified as having high strain (high demands and low control) and having occupational noise exposure >75 dB(A), the risk for coronary heart disease further increased; HR 1.80 (95% CI 1.19-2.73, age adjusted and

risk factor adjusted; HR 1.73 (95% CI 1.14-2.61. The interaction analyses regarding stroke were negative.

Table 3. Interaction between occupational noise exposure and high strain. Hazard ratios (HR) with confidence intervals for coronary heart disease and stroke in subjects exposed for high strain versus not exposed for high strain in relation to exposure for occupational noise among all men (n=5753).

	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)

	High strain	Not high strain	High strain	Not high strain
Coronary heart disease n=1004 events	<75 dB(A) n=29 >=75 dB(A) n=99	<75 dB(A) n=451 >=75 dB(A) n=425		
Low noise, <75 dB(A)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium and high noise, >=75 dB(A)	1.80 (1.19-2.73)	1.10 (0.96-1.25)	1.73 (1.14-2.61)	1.08 (0.94-1.23)
p for interaction	p=0.03		p=0.03	
	unlikely n=92 maybe n=23 likely n=13	unlikely n=530 maybe n=112 likely n=234		
Noise peaks unlikely	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	1.39 (0.88-2.19)	1.00 (0.81-1.22)	1.45 (0.91-2.29)	0.99 (0.80-1.21)
Noise peaks likely	1.25 (0.70-2.23)	1.20 (1.03-1.40)	1.29 (0.72-2.31)	1.16 (0.99-1.35)
p for interaction	p=0.43		p=0.32	
Stroke n=517 events	<75 dB(A) n=17 >=75 dB(A) n=43	<75 dB(A) n=245 >=75 dB(A) n=212		
Low noise, <75 dB(A)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium and high noise, >=75 dB(A)	1.33 (0.76-2.33)	1.01 (0.84-1.21)	1.38 (0.79-2.43)	0.98 (0.82-1.19)
p for interaction	p=0.35		p=0.27	
	unlikely n=47 maybe n=6 likely n=7	unlikely n=289 maybe n=53 likely n=115		
Noise peaks unlikely	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	0.68 (0.29-1.60)	0.86 (0.64-1.15)	0.70 (0.30-1.65)	0.85 (0.64-1.15)
Noise peaks likely	1.44 (0.65-3.19)	1.07 (0.87-1.33)	1.34 (0.61-2.98)	1.04 (0.84-1.30)
p for interaction	p=0.66		p=0.74	

*age in years, baseline BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25), baseline diabetes, hypertension and by stratification never/ever smoker, cholesterol in quartiles

Discussion

The present study shows an increased risk for coronary heart disease in relation to both continuous noise and peaks of occupational exposure to noise, concomitant exposure for high strain further increased the risk of CHD. There was no increased risk for stroke in relation to occupational noise exposure.

This study has several advantages such as high external validity because a general-population sample with a long period of follow-up was available and near complete follow up. The use of a national mortality register and hospital discharge register with high coverage further increase the validity of the results.

However, there are also several limitations. Regarding the stroke outcome, the restricted number of cases and lack of computerized tomography during early follow up did not allow for analyses of subtypes of stroke so there may be a misclassification. Stroke comprises different subtypes such as ischemic stroke, intra-cerebral bleeding and sometimes also sub-arachnoidal bleeding is included in the stroke concept. All those clinical subtypes of stroke may have different risk factors. In a Japanese study (12) comprising 14568 subjects, the hazard ratio for intra-cerebral bleeding was 2.1 (1.01-4.4) and the hazard ratio for ischemic stroke was 1.7 (0.7-4.1). The noise levels were self-reported and the outcome was based on population registries.

There were no individual measurements of noise levels for the participants; instead the assigned exposure was estimated from average levels in similar work places using a previously developed noise JEM. In a Swedish case control study where the subjects occupational noise exposure was classified using the same job-exposure matrix as in our study there was an increased odds ratio for myocardial infarction for occupational noise exceeding 75 dB(A), but with adjustments for age, sex, smoking, socioeconomic status and air pollution the risk decreased and became insignificant (20). The assessment of noise exposure and job-strain based on job exposure matrices may display less bias than self-reports. But there may be a considerable non-differential misclassification of the exposure estimates causing attenuation of the risk estimates.

We did not have information regarding individual use of hearing protection but most of the men in the cohort retired from work at the latest at the end of the 1980s and in Sweden the use of hearing protection became commonly used first at that time. It is not likely that there has been a frequent use of hearing protection among the subjects. Also, we did not have information regarding co-exposures such as dust, fumes or residential noise. Of importance is also that the study comprises only men which limits its external validity.

We had access to individual baseline data regarding smoking habits, BMI, diabetes, hypertension, and cholesterol; this made it possible to have control of interactions and confounding. A 18-year follow-up of 6005 men from the Helsinki Heart Study where they

also had access to register-based outcome and individual data on smoking, BMI and blood pressure also showed an increased risk, 1.48 (95% CI 1.28-1.71) of coronary heart disease in relation to continuous noise exposure exceeding 85 dB(A), exposure to impulse noise showed similar risk estimates. (10).

In general, we have simple, only age adjusted models as risk factors can be mediators, but we also present risk factor adjusted models. A sensitivity analysis was also performed, the cohort was analysed without the subjects with baseline hypertension and diabetes, a significantly increased risk with a positive trend remained for coronary heart disease. We did not have socioeconomic status and adjusting for it could implicate an over-adjustment; the exposure is based on occupations, which usually comprise the socioeconomic position.

We used the job held at the age of 50 years, which probably in most cases reflects the longest held job. We also analysed the risk below 65 years and found higher risks in working age. This may reflect that the risk of coronary heart disease is dependent on current noise exposure and that the risk may decrease after termination of the work as observed in the Canadian study (10) where the highest risk was found among those who were currently working and had been employed 20 years or more with relative risks between 2.0 and 4.0.

Our results showed an interaction between noise and high strain. However there are also reported interactions between job-strain and life-style factors like smoking, being obese or reporting low physical activity (29). We have adjusted for smoking and BMI, but not physical activity as we do not have this information.

Our results regarding coronary heart disease corroborate earlier studies, giving further evidence for a causal relation between occupational noise exposure and increased risk for coronary heart disease (4-8). We also support the findings by Selander et al that high strain (high demand/low control) further increased the risk for coronary heart disease (20). The results from the present study indicate that exposure to occupational noise is not increasing the risk for stroke in accordance with previous studies (13, 15). This could be due to power, suboptimal classification of the different subtypes of stroke or perhaps that stroke has a different pattern of occupational risk factors compared to coronary heart disease.

Conclusions

Exposure to occupational noise increased the risk for coronary heart disease. There was no increased risk for stroke in any of the noise exposure categories. There were indications of an

interaction between noise exposure and work-related strain, and further studies are needed to elucidate patterns of interactions between different occupational risk factors.

References

1. Socialstyrelsen. Statistik om stroke, korta fakta (Internet). Downloaded from: http://www.socialstyrelsen.se/statistik/statistikefteramne/hjartinfarkter
2. Socialstyrelsen. Statistik om stroke, korta fakta (Internet). Downloaded from: http://www.socialstyrelsen.se/statistik/statistikefteramne/stroke
3. Lie A, Skogstad M, Johannessen H. Occupational noise exposure and hearing: a systematic review *Int Arch Occup Environ Health*. 2016;89:351-72.
4. Sbihi H1, Davies HW, Demers PA. Hypertension in noise-exposed sawmill workers: a cohort study. *Occup Environ Med*. 2008;65:643-46.
5. Skogstad M, Johannessen HA, Tynes T et al. Systematic review of the cardiovascular effects of occupational noise. *Occup Med* 2016;66:10-16.
6. Skogstad M, Johannessen HA, Tynes T et al. Corrigendum Systematic review of the cardiovascular effects of occupational noise. *Occup Med* 2016;66:10-16.
7. Theorell T, Jood K, Järvholm LS et al. A systematic review of studies in the contributions of the work environment to ischaemic heart disease development. *Eur J Public Health* 2016;26:470–77.
8. Dzhambov AM, Dimitrova DD. Occupational noise and ischemic heart disease: A systematic review. *Noise Health*. 2016;18:167-77.
9. Kolstad HA, Stokholm Z, Hansen ÅM et al. Whether noise exposure causes stroke or hypertension is still not known. *BMJ* Online [eLetter] 16 December 2013. http://www.bmj.com/content/347/bmj.f7444.long
10. Davies HW, Teschke K, Kenedy SM et al. Occupational exposure to noise and mortality from acute myocardial infarction. *Epidemiology* 2005;16:25-32.
11. Virkkunen H, Kauppinen T, Tenkanen L. Long-term effect of occupational noise on the risk of coronary heart disease. *Scand J Work Environ Health* 2005;31:291-299.
12. Fujino Y, Iso H, Tamakoshi A, for the JACC study group. A prospective cohort study of perceived noise exposure at work and cerebrovascular diseases among male workers in Japan. *J Occup Health* 2007;49:382-388.
13. Stokholm ZA, Bonde JP, Christensen KL et al. Occupational noise exposure and the risk of stroke. *Stroke* 2013;44:3214-3216.
14. Gopinath B, Thiagalingam A, Teber E, Mitchell P. Exposure to workplace noise and the risk of cardiovascular disease events and mortality among older adults. Prev Med 2011;53:390-394.

15. Dzhambov AM, Dimitrova DD, Tokmakova MP. Association between self-reported occupational noise and the prevalence of stroke: Secondary analysis of the National Health Interview Survey, 2014. Noise Control Engineering Journal. 2016;64:779-788.
16. Basner M, Babisch W, Davis A et al. Auditory and non auditory effects of noise on health. *Lancet* 2014;383:1325-1332.
17. Karasek RA. Job demands, job decision latitude, and mental strain: Implications for job redesign. *Admin Sci Qtrly* 1979;24:285-308.
18. Eller NH, Netterstrøm B, Gyntelberg F et al. Work-related psychosocial factors and the development of ischemic heart disease: a systematic review. *Cardiol Rev* 2009;17:83-97.
19. Kivimäki M, Nyberg ST, Batty GD et al. Job strain as a risk factor for coronary heart disease: A collaborative meta-analysis of individual participant data. *Lancet* 2012;380:1491-1497.
20. Selander J, Bluhm G, Nilsson M et al. Joint effects of job strain and road-traffic and occupational noise on myocardial infarction. *Scand J Work Env Health* 2013;39:195-203.
21. Wilhelmsen L, Berglund G, Elmfeldt D et al. The multifactor primary prevention trial in Goteborg, Sweden. *Eur Heart J* 1986;7:279-288.
22. Harmsen P, Lappas G, Rosengren A et al. Long-term risk factors for stroke: Twenty-eight years of follow-up of 7457 middle-aged men in Göteborg, Sweden. *Stroke* 2006; 37:1663-1667.
23. Torén K, Schiöler L, Söderberg M et al. The association between job strain and atrial fibrillation in Swedish men. *Occup Environ Med* 2015;72:177-180.
24. Sjöström M, Lewné M, Alderling M et al. A job-exposure matrix for occupational noise: Development and validation. *Ann Occup Hyg* 2013;57:774-783.
25. Johnson JV, Stewart W, Hall EM et al. Long-term psychosocial work environment and cardiovascular mortality among Swedish men. *Am J Public health* 1996;86:324-331.
26. Fredlund P, Hallqvist J, Diderichsen F. Psykosocial yrkesexponeringsmatris. *Arbete och Hälsa* 2000;11:1-37 [In Swedish].
27. Torén K, Schiöler L, Giang WK et al. A longitudinal general population-based study of job strain and risk for coronary heart disease and stroke in Swedish men. *BMJOpen* 2014;4:e004355

28. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika* 1994;81:515-526.
29. Kivimäki M, Nyberg ST, Fransson EI et al. Associations of job strain and lifestyle factors with risk of coronary artery disease: A meta-analysis of individual participant data. *Can Med Assoc J* 2013;185:763-769.

- **Contributors**: Rosengren, Torén, Andersson conceptualized, designed and supervised the study. Eriksson helped to conceive the study and drafted the manuscript. Sjöström has participated in developing the job exposure matrix regarding noise. Schiöler performed the statistical analyses. Söderberg critically revised the manuscript. All authors were responsible for the drafting of the manuscript and for the final approval of the manuscript.

- **Funding**: The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation.

- **Competing interests**: None. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: *no support from any organisation for the submitted work*; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work

- **Ethics statement**: Ethics approval by the Ethics Committee for Medical Research at the University of Gothenburg.

- **Provenance and peer review**: Not commissioned; externally peer reviewed.

- **Data sharing statement**: This is a large general population study which has been followed for many years. There are unpublished data in the dataset. Scientific cooperation around this study is possible by contacting the corresponding author.

STROBE. **A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men.** 2017-08-14. Helena Eriksson.

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract YES
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found YES
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported YES
Objectives	3	State specific objectives, including any prespecified hypotheses YES
Methods		
Study design	4	Present key elements of study design early in the paper YES
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection YES
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. YES *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. YES
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. YES
Bias	9	Describe any efforts to address potential sources of bias. YES
Study size	10	Explain how the study size was arrived at. YES
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. YES
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding. YES
		(*b*) Describe any methods used to examine subgroups and interactions. YES
		(*c*) Explain how missing data were addressed. YES
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed. YES *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. YES
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. YES
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount). YES
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time YES
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. YES
		(*b*) Report category boundaries when continuous variables were categorized. YES
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses. YES
Discussion		
Key results	18	Summarise key results with reference to study objectives. YES
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. YES
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. YES
Generalisability	21	Discuss the generalisability (external validity) of the study results. YES
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. YES

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019160.R2
Article Type:	Research
Date Submitted by the Author:	25-Jan-2018
Complete List of Authors:	Eriksson, Helena; Sahlgrenska universitetssjukhuset, Department of Occupational and Environmental Medicine; Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Section of Occupational and Environmental Medicine Andersson, Eva; Goteborgs Universitet, 4. Occupational and Environmental Medicine, Institute of Medicine, The Sahlgrenska Academy Schiöler, Linus; Medicine, Occupational and environmental medicine Söderberg, Mia; Medicine, Occupational and environmental medicine Sjöström, Mattias; Karolinska Institutet, Institute of Environmental Medicine Rosengren, Annika; Sahlgrenska University HospitalOstra Torén, Kjell; Sahlgrenska universitetssjukhuset, Occupational and Environmental medicine; Goteborgs universitet Sahlgrenska Akademin, Section of Occupational and Environmental Medicine, Institute of Medicine
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	OCCUPATIONAL & INDUSTRIAL MEDICINE, Coronary heart disease < CARDIOLOGY, EPIDEMIOLOGY

A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men.

Helena Eriksson[1], Eva Andersson[1], Linus Schiöler[2], Mia Söderberg[2], Mattias Sjöström[3, 4], Annika Rosengren[5], Kjell Torén[1, 2]

1. Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden.
2. Section of Occupational and Environmental Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden.
3. Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.
4. Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden.
5. Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden.

Corresponding author: Helena Eriksson, Department of Occupational and Environmental Medicine, Sahlgrenska University Hospital, Box 414, S-405 30 Gothenburg, Sweden.
E-mail: helena.eriksson@amm.gu.se

Word count: abstract 295, main text 2622.

Abstract

Objectives: The aim was to investigate whether occupational noise increased the risk for coronary heart disease and stroke and to elucidate interactions with stressful working conditions in a cohort of Swedish men.

Design: Prospective cohort study of Swedish men followed until death, hospital discharge or until 75 years of age regarding coronary heart disease (CHD) and stroke, using Swedish national registers on cause of death and hospital discharges. Baseline data on occupation from 1974-77, was used for classification of levels of occupational noise and job demand-control. Cox regression was used to analyse the hazard ratios, HR, for CHD and stroke.

Setting: Swedish men born 1915-1925

Primary and secondary outcome measures: Coronary heart disease and stroke

Participants: Men from the Primary Prevention Study, a random sample of 10 000 men born 1915-1925 in Gothenburg. Subjects with coronary heart disease or stroke at baseline or not employed were excluded. The remaining subjects with complete baseline data on occupation, weight, height, hypertension, diabetes, serum cholesterol and smoking constituted the study sample, 5753 men.

Results

There was an increased risk for CHD in relation to noise levels 75-85 dB(A) and >85 dB(A) compared to <75 dB(A), HR 1.15 (95% CI 1.01-1.31) and HR 1.27 (95% CI 0.99-1.63), respectively. Exposure to noise peaks also increased the risk for CHD (HR 1.19, 95% CI 1.03-1.38). Among those with high strain (high demands and low control) combined with noise >75 dB(A), the risk for CHD further increased; HR 1.80 (95% CI 1.19-2.73). There was no significantly increased risk for stroke in any noise category.

Conclusions

Exposure to occupational noise was associated with an increased risk for CHD and the risk further increased among those with concomitant exposure for high strain. None of the analysed variables were related to increased risk for stroke.

Keywords: Noise, strain, IHD, CVD

Strengths and limitations of this study

Longitudinal cohort study with long-term follow up which strengthens the results

Data was retrieved from national mortality register and hospital discharge register with high coverage, which increases the validity

Noise exposure was classified through a job exposure matrix but no individual measurements of noise were performed

Only men in the cohort, which limits the generalizability

Introduction

Cardiovascular diseases are common diseases in Sweden as in most countries, in 2016, 25700 persons suffered from acute myocardial infarction and 25% of these died within 28 days (1). In the same year stroke occurred in 26500 persons and of these, 26% died within 28 days (2).

Exposure to noise is frequent in many workplaces, and health effects, especially hearing disorders have been investigated since decades (3). In addition to the hearing effects, there are studies indicating that occupational exposure to noise may increase the risk for cardiovascular diseases, such as hypertension, coronary heart disease and stroke (4-8). The evidence is, however, rather weak, especially regarding the association with stroke where there is a conspicuous lack of prospective studies (9). Regarding coronary heart disease and occupational exposure to noise, the few available longitudinal studies seem to favour an association. In a Canadian study of 30 000 lumber mill workers, there was an increased risk of fatal acute myocardial infarction both in relation to duration of employment and in relation to noise levels (10). A Finnish study showed an increased risk for coronary heart disease in relation to continuous noise exposure exceeding 85 dB(A), impulse noise also showed an increased risk (11).

There are few studies and there is conflicting evidence whether occupational exposure to noise increases the risk for stroke (9). A Japanese study (12) showed an increased hazard ratio for intra-cerebral bleeding but not for ischemic stroke. A Danish study (13) of more than 200000 workers did not show an increased risk of stroke in relation to occupational noise exposure. In an Australian study of 2942 subjects, there was a significant association between the incidence of stroke and those exposed to very high levels of noise (14).

In a study from 2016 based on noise exposure and occurrence of stroke in the US general population there was no statistically significant association between exposure for noise and stroke after adjustment for sociodemographics, lifestyle and comorbidity (15).

The mechanisms regarding occupational noise exposure and risk for cardiovascular disease are not clear. Environmental noise and the mechanisms behind the increased risk for cardiovascular disease has been studied to a larger extent (16). Noise exposure activates the autonomic and endocrine systems, the blood pressure increases, the heart rate is altered and stress hormones are released. Chronic noise exposure can affect blood pressure, blood glucose, blood lipids and viscosity leading to an increased risk for cardiovascular disease (16).

Exposure to work-place stress is often evaluated according to the job-demand-control model (17). Throughout the literature, high strain, the combination of high demands and low control, has been linked to ill-health primarily coronary heart disease (18). A recent meta-analysis of 13 studies concluded that the association to coronary heart disease was rather small but consistent, hazard ratio 1.23 (19). However, there seems to be interactions between job-strain and occupational noise (20).

The aim of the present study was to investigate whether occupational exposure to noise increased the risk for coronary heart disease and stroke, and to elucidate potential interactions with stressful psychosocial work conditions based on the job-demand-control model in a longitudinal general population study.

Methods

Study population

The Primary Prevention Study (PPS) is a cohort study obtained from a general-population sample as previously described (21, 22). The source population comprised 10 000 men, a random third of all men living in Gothenburg born between 1915 and 1925, of whom 7494 participated in screening examinations between January 1970 and March 1973. Three years later, 1974-1977, a clinical follow-up investigation was performed where 7 133 men participated. In the present study we used the follow-up data as our baseline since it includes occupational data and information about age, body mass index BMI, (BMI is the weight in kilograms divided by the square of the body height in meters), serum cholesterol (s-cholesterol) level, systolic blood pressure, diastolic blood pressure, physician diagnosed diabetes (yes/no), physician diagnosed hypertension (yes/no), coronary heart disease (yes/no) or stroke (yes/no) and smoking as previously described (23).

Subjects with coronary heart disease or stroke at baseline (n=329) and subjects not employed (n=730) were excluded, leaving 6074. The remaining subjects with complete baseline data on occupation, weight, height, hypertension, diabetes, serum cholesterol and smoking constituted the study sample, (n=5753) with an age range of 50-59 years (Table 1). All participants gave their informed consent to participate in the study and it was approved by the Regional Ethical Review Board, Gothenburg University, Sweden.

Table 1. Baseline characteristics of 5753 Swedish men in a general population study, by different noise exposure levels.

	Low exposure <75 dB(A) n=2930	Medium exposure 75-85dB(A) n=2467	High exposure >85dB(A) n=356	Noise peaks unlikely n=3718	Noise peaks maybe n=757	Noise peaks likely n=1278	Overall n=5753
Mean age, yrs (SD)	55.2 (2.1)	55.3 (2.0)	55.3 (2.0)	55.3 (2.1)	55.2 (2.0)	55.3 (2.0)	55.3 (2.1)
Mean cholesterol, mmol/L (SD)	6.4 (1.04)	6.4 (1.04)	6.4 (1.12)	6.4 (1.04)	6.4 (1.09)	6.4 (1.04)	6.4 (1.05)
Mean SBP, mm Hg (SD)	145.3 (19.6)	146.3 (19.6)	146.1 (19.6)	145.7 (19.6)	145.4 (19.1)	146.4 (19.8)	145.8 (19.6)
Mean BMI, kg/m^2 (SD)	25.4 (3.1)	25.8 (3.3)	25.8 (3.0)	25.5 (3.2)	25.5 (3.1)	25.9 (3.3)	25.6 (3.2)
BMI <18.5, % (n)	0.5% (n=15)	0.3% (n=8)	0.3% (n=1)	0.5% (n=18)	0.3% (n=2)	0.3% (n=4)	0.4% (n=24)
BMI 18.5-<25, % (n)	47.0% (n=1376)	43.0% (n=1061)	40.2% (n=143)	46.1% (n=1712)	45.7% (n=346)	40.9% (n=522)	44.9% (n=2580)
BMI 25-<30, % (n)	45.3% (n=1328)	47.1% (n=1163)	50.0% (n=178)	45.4% (n=1687)	45.6% (n=345)	49.8% (n=637)	46.4% (n=2669)
BMI >=30 %, (n)	7.2% (n=211)	9.5% (n=235)	9.6% (n=34)	8.1% (n=301)	8.5% (n=64)	9.0% (n=115)	8.3% (n=480)
Diabetes, % (n)	2.7% (n=80)	2.9% (n=71)	3.4% (n=12)	2.8% (n=105)	3.3% (n=25)	2.6% (n=33)	2.8%(n=163)
Hypertension, % (n)	21.5% (n=629)	22.3% (n=551)	21.6% (n=77)	21.7% (n=808)	19.9% (n=151)	23.3% (n=298)	21.8% (n=1257)
Ever smoker, % (n)	73.3% (n=2148)	76.8% (n=1894)	77.8% (n=277)	74.3% (n=2763)	72.8% (n=551)	78.6%(n=1005)	75.1% (n=4319)
High strain, % (n)	7.3% (n=215)	16.7% (n=413)	9.6% (n=34)	13.8% (n=512)	12.0% (n=91)	4.6% (n=59)	11.5% (n=662)

BMI is the weight in kilograms divided by the square of the body height in meters.

For assessing occupational noise exposure, a previously developed job-exposure matrix (JEM) regarding noise was applied (24). The noise JEM is based on 145 measurement reports and a total of 569 measurements on 129 unique job families. It classifies 321 occupations based on the NYK -85/90 according to noise levels and peak levels. The noise JEM classification is covering the period from 1970 to 2004 in five-year intervals.

The noise levels were categorized into three different levels, low; <75 dB(A), medium; 75-85 dB(A) and high; > 85 dB(A) in the JEM. There was also an assessment of whether there was a high risk of peak level noise exposure and the categories: 'Noise peaks likely' ('Yes, for sure' combined with 'Yes, probably') and 'Noise peaks maybe' was compared with the category 'Noise peaks unlikely'.

For assessing the psychosocial workplace exposure, we used a previously published and used job-exposure matrix (25, 26). This psychosocial JEM provides separate estimates of job demand and control for 261 occupations separated into gender and age (25 to 44 and 45 to 74) as previously described (23, 27). Job demands and decision latitude were explored with four items each, and all subjects were assigned a certain score based on occupation and age in this psychosocial JEM. Using the median of the distribution as cut-off, which is standard procedure, demand and control were dichotomized as high or low. The participants were then allocated into four categories; high strain (high demand-low control), active (high demand-high control), passive (low demand-low control) and low-strain (low demand-high control).

Based on Sweden's unique personal identification numbers, participants were followed from the date of their baseline examination until death, until hospital discharge or until 75 years of age, using the Swedish national register on cause of death and the Swedish hospital discharge register.

All discharges from Gothenburg hospitals have been entered into the national register since 1970, with the exception of 1976. The outcomes were classified according to ICD-8 code until 1986, ICD-9 was used from 1987 to 1996, and ICD-10 was used from 1997 onwards. Coronary heart disease was defined as 410-414 (ICD-8, 9) and as I20-I25 (ICD-10) from the death register and as acute myocardial infarction 410 and I21 from the discharge register, respectively. Stroke events, including both ischemic stroke and intracerebral bleeding, were defined as death or hospitalisation with ICD codes 431-438 (ICD-8, 9) and I61-I69 (ICD-10). Each type of event was treated separately and only the first event of each type was used in the analysis.

Statistical analysis

Descriptive statistics are presented as percentages or mean values with standard deviations (SD). All analyses were performed using the SAS statistical package (version 9.3) and R (version 3.0.1). The material was analysed with Cox regression models using SAS (the PHREG procedure). The proportional hazards assumptions were investigated using tests and plots based on weighted residuals (28) using the R package Survival. Proportional hazards assumptions were found reasonable except for the analysis of smoking and serum cholesterol, which we stratified for in the risk factor adjusted models. Hospital care or mortality (whatever came first) from coronary heart disease or stroke were considered events and time were measured as months since baseline. The observation period stopped at the age of 75. Analyses were also performed restricted to subjects younger than 65 years. In the crude models hazard ratios (HR) and 95% confidence intervals (CI) were calculated using the occupational noise exposure and age as explanatory variables. Tests for trend were performed by including the covariate as a continuous variable.

In the risk factor adjusted models we adjusted for ever-smoking (yes/no), cholesterol (quartiles), history of diabetes (yes/no), hypertension (yes/no), and BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25). Interaction between occupational noise exposure and high strain was analysed separately, here the noise exposure was aggregated into <75 and >75 dB(A) to gain power. The population was divided in two groups, subjects exposed for high strain versus others not exposed for high strain and hazard ratios were calculated. Wald test was used to test interaction.

A sensitivity analysis was performed restricted to the subjects without hypertension and diabetes, potential mediators for coronary heart disease.

Results

During the follow-up period of totally 94222 person-years (mean years per person 16.4) there were 1004 events of coronary heart disease (Table 2). The Cox regression models adjusted for age showed an increased hazard ratio for coronary heart disease in relation to medium levels (HR 1.15, 95% CI 1.01-1.31) and high levels (HR 1.27, 95% CI 0.99-1.63) of occupational noise exposure (Table 2) and a positive trend.

Table 2. Incidence and Hazard Ratios (HR) with confidence intervals (CI) for coronary heart disease and stroke in relation to exposure for occupational noise among all men (n=5753).

	Events per 1000 observation years (n events)	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)
Coronary heart disease, all	10.7 (n=1004)		
Low noise, <75 dB(A)	9.8 (n=480)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	11.4 (n=453)	1.15 (1.01-1.31)	1.13 (0.99-1.28)
High noise, >85 dB(A)	12.4 (n=71)	1.27 (0.99-1.63)	1.22 (0.95-1.56)

	Events per 1000 observation years (n events)	Age adjusted HR (95% CI)	Risk factor adjusted* HR (95% CI)
Noise peaks unlikely	10.2 (n=622)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	10.6 (n=135)	1.05 (0.87-1.26)	1.04 (0.86-1.25)
Noise peaks likely	12.1 (n=247)	1.19 (1.03-1.38)	1.16 (1.00-1.34)
p for trend		p=0.03	p=0.06
Stroke, all	5.4 (n=517)		
Low noise, <75 dB(A)	5.3 (n=262)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	5.4 (n=220)	1.02 (0.85-1.22)	1.01 (0.84-1.21)
High noise, >85 dB(A)	6.0 (n=35)	1.16 (0.82-1.65)	1.12 (0.79-1.59)
p for trend		p=0.51	p=0.65
Coronary heart disease, subjects ≤65 years	7.5 (n=375)		
Noise peaks unlikely	5.4 (n=336)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	4.5 (n=59)	0.83 (0.63-1.10)	0.84 (0.63-1.10)
Noise peaks likely	5.8 (n=122)	1.08 (0.88-1.33)	1.06 (0.86-1.30)
p for trend		p=0.65	p=0.82
Low noise, <75 dB(A)	6.7 (n=174)	1.00 (ref)	1.00 (ref)
Medium noise, 75-85 dB(A)	8.2 (n=172)	1.20 (0.97-1.48)	1.17 (0.94-1.44)
High noise, >85 dB(A)	9.4 (n=29)	1.38 (0.93-2.05)	1.30 (0.88-1.93)
p for trend		p=0.04	p=0.09
Stroke, subjects ≤65 years	2.7 (n=138)		
Noise peaks unlikely	2.8 (n=73)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	2.1 (n=41)	0.82 (0.58-1.13)	0.82 (0.59-1.14)
Noise peaks likely	3.3 (n=91)	1.11 (0.87-1.41)	1.07 (0.84-1.36)
p for trend	7.5 (n=243)	p=0.60	p=0.81

Medium noise, 75-85 dB(A)	2.5 (n=54)	0.89 (0.63-1.27)	0.90 (0.63-1.28)
High noise, >85 dB(A)	3.5 (n=11)	1.26 (0.67-2.37)	1.23 (0.65-2.32)
p for trend		p=0.97	p=0.98
Noise peaks unlikely	2.7 (n=89)	1.00 (ref)	1.00 (ref)
Noise peaks maybe	1.8 (n=12)	0.65 (0.36-1.19)	0.66 (0.36-1.20)
Noise peaks likely	3.3 (n=37)	1.23 (0.84-1.81)	1.23 (0.83-1.80)
p for trend		p=0.46	p=0.47

*age in years, baseline BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25), baseline diabetes, hypertension and by stratification never/ever smoker, cholesterol in quartiles.

Exposure to noise peaks also increased the risk for coronary heart disease (HR 1.19, 95% CI 1.03-1.38). In the risk factor adjusted models all estimates were slightly diminished but regarding noise peaks the statistical significance remained. When the risk for coronary heart disease was restricted to subjects younger than 65 years, the risk estimates increased, but due to lack of power the confidence intervals turned wider and included unity.

When analyzing the cohort without the subjects with hypertension and diabetes at baseline (n=4400), the HR for coronary heart disease was 1.20 (95% CI 1.03-1.41) in relation to medium level of noise exposure and HR 1.49 (95% CI 1.11-1.99) in relation to high level of noise exposure and for the subjects with likely exposure for noise peaks the HR was 1.30 (95% CI 1.09-1.55).

In the follow-up period, there were 517 stroke events. There was no increased risk for stroke in any of the exposure strata, medium levels, high levels or peaks of noise exposure (Table 2).

In Table 3, risk estimates for occupational noise exposure are outlined in the different groups of high strain and not high strain. Among those who were classified as having high strain (high demands and low control) and occupational noise exposure >75 dB(A), the risk for coronary heart disease further increased; HR 1.80 (95% CI 1.19-2.73), age adjusted and risk factor adjusted; HR 1.73 (95% CI 1.14-2.61). The interaction analyses regarding stroke were negative.

	Age adjusted HR	Risk factor adjusted*

Table 3. Interaction between occupational noise exposure and high strain. Hazard ratios (HR) with confidence intervals for coronary heart disease and stroke in subjects exposed for high strain versus not exposed for high strain in relation to exposure for occupational noise among all men (n=5753).

	(95% CI)		HR (95% CI)	
	High strain (n events)	**Not high strain (n events)**	**High strain**	**Not high strain**
Coronary heart disease, all, n=1004 events				
Low noise, <75 dB(A)	1.00 (ref) n=29	1.00 (ref) n=451	1.00 (ref)	1.00 (ref)
Medium and high noise, >=75 dB(A)	1.80 (1.19-2.73) n=99	1.10 (0.96-1.25) n=425	1.73 (1.14-2.61)	1.08 (0.94-1.23)
p for interaction	p=0.03		p=0.03	
Noise peaks unlikely	1.00 (ref) n=92	1.00 (ref) n=530	1.00 (ref)	1.00 (ref)
Noise peaks maybe	1.39 (0.88-2.19) n=23	1.00 (0.81-1.22) n=112	1.45 (0.91-2.29)	0.99 (0.80-1.21)
Noise peaks likely	1.25 (0.70-2.23) n=13	1.20 (1.03-1.40) n=234	1.29 (0.72-2.31)	1.16 (0.99-1.35)
p for interaction	p=0.43		p=0.32	
Stroke, all, n=517 events				
Low noise, <75 dB(A)	1.00 (ref) n=17	1.00 (ref) n=245	1.00 (ref)	1.00 (ref)
Medium and high noise, >=75 dB(A)	1.33 (0.76-2.33) n=43	1.01 (0.84-1.21) n=212	1.38 (0.79-2.43)	0.98 (0.82-1.19)
p for interaction	p=0.35		p=0.27	
Noise peaks unlikely	1.00 (ref) n=47	1.00 (ref) n=289	1.00 (ref)	1.00 (ref)
Noise peaks maybe	0.68 (0.29-1.60) n=6	0.86 (0.64-1.15) n=53	0.70 (0.30-1.65)	0.85 (0.64-1.15)
Noise peaks likely	1.44 (0.65-3.19) n=7	1.07 (0.87-1.33) n=115	1.34 (0.61-2.98)	1.04 (0.84-1.30)
p for interaction	p=0.66		p=0.74	

*age in years, baseline BMI (<18.5, 25-<30 and =>30 compared to 18.5-<25), baseline diabetes, hypertension and by stratification never/ever smoker, cholesterol in quartiles

Discussion

The present study suggests an increased risk for coronary heart disease in relation to both continuous noise and peaks of occupational exposure to noise, concomitant exposure to high strain further increased the risk of CHD. There was no increased risk for stroke in relation to occupational noise exposure.

This study has several advantages such external validity because a general-population sample with a long period of follow-up was available with near complete follow up. The use of a national mortality register and hospital discharge register with high coverage further increased the validity of the results.

However, there are also several limitations. Regarding the stroke outcome, the restricted number of cases and lack of computerized tomography during early follow up did not allow for analyses of subtypes of stroke so there may be a misclassification. Stroke comprises different subtypes such as ischemic stroke, intra-cerebral bleeding and sometimes also sub-arachnoidal bleeding is included in the stroke concept. All those clinical subtypes of stroke may be related to different risk factors. In a Japanese study (12) comprising 14568 subjects, the hazard ratio for intra-cerebral bleeding was 2.1 (1.01-4.4) and the hazard ratio for ischemic stroke was 1.7 (0.7-4.1). The noise levels were self-reported and the outcome was based on population registries.

There were no individual measurements of noise levels for the participants; instead the assigned exposure was estimated from average levels in similar work places using a previously developed noise JEM. In a Swedish case control study where the subjects occupational noise exposure was classified using the same job-exposure matrix as in our study there was an increased odds ratio for myocardial infarction for occupational noise exceeding 75 dB(A), but with adjustments for age, sex, smoking, socioeconomic status and air pollution the risk decreased and became insignificant (20). The assessment of noise exposure and job-strain based on job exposure matrices may display less bias than self-reports. But there may be a considerable non-differential misclassification of the exposure estimates causing attenuation of the risk estimates.

We did not have information regarding individual use of hearing protection but most of the men in the cohort retired from work at the latest at the end of the 1980s and in Sweden the use of hearing protection became commonly used first at that time. It is not likely that there has been a frequent use of hearing protection among the subjects. In addition, we did not have

information regarding co-exposures such as dust, fumes or residential noise. Of importance is also that the study comprises only men, which limits its external validity.

We had access to individual baseline data regarding smoking habits, BMI, diabetes, hypertension, and cholesterol; this made it possible to have control of interactions and confounding. A 18-year follow-up of 6005 men from the Helsinki Heart Study where they also had access to register-based outcome and individual data on smoking, BMI and blood pressure showed an increased risk, 1.48 (95% CI 1.28-1.71) of coronary heart disease in relation to continuous noise exposure exceeding 85 dB(A), exposure to impulse noise showed similar risk estimates (10).

In general, we have simple, only age adjusted models as risk factors can be mediators, but we also present risk factor adjusted models. A sensitivity analysis was also performed, and a significantly increased risk of coronary heart disease remained when excluding the subjects with baseline hypertension and diabetes. We did not have socioeconomic status and adjusting for it could implicate an over-adjustment; the exposure was based on occupations, which usually comprise the socioeconomic position.

We used the job held at the age of 50 years, which probably in most cases reflects the longest held job. We also analysed the risk below 65 years and found higher risks in working age. This may reflect that the risk of coronary heart disease is dependent on current noise exposure and that the risk may decrease after termination of the work as observed in the Canadian study (10) where the highest risk was found among those who were currently working and had been employed 20 years or more with relative risks between 2.0 and 4.0.

Our results showed an interaction between noise and high strain. However there are also reported interactions between job-strain and life-style factors like smoking, being obese or reporting low physical activity (29). We have adjusted for smoking and BMI, but not physical activity, as we do not have this information.

Our results regarding coronary heart disease corroborate earlier studies, giving further evidence for a causal relation between occupational noise exposure and increased risk for coronary heart disease (4-8). We also support the findings by Selander et al that high strain (high demand/low control) further increased the risk for coronary heart disease (20). The results from the present study indicate that exposure to occupational noise is not increasing the risk for stroke in accordance with previous studies (13, 15). This could be due to power,

suboptimal classification of the different subtypes of stroke or perhaps that stroke has a different pattern of occupational risk factors compared to coronary heart disease.

Conclusions

Exposure to occupational noise increased the risk of coronary heart disease. There was no increased risk for stroke in any of the noise exposure categories. There were indications of an interaction between noise exposure and work-related strain, and further studies are needed to elucidate patterns of interactions between different occupational risk factors.

References

1. Socialstyrelsen. Statistik om stroke, korta fakta (Internet). Downloaded from: http://www.socialstyrelsen.se/statistik/statistikefteramne/hjartinfarkter
2. Socialstyrelsen. Statistik om stroke, korta fakta (Internet). Downloaded from: http://www.socialstyrelsen.se/statistik/statistikefteramne/stroke
3. Lie A, Skogstad M, Johannessen H. Occupational noise exposure and hearing: a systematic review *Int Arch Occup Environ Health*. 2016;89:351-72.
4. Sbihi H1, Davies HW, Demers PA. Hypertension in noise-exposed sawmill workers: a cohort study. *Occup Environ Med*. 2008;65:643-46.
5. Skogstad M, Johannessen HA, Tynes T et al. Systematic review of the cardiovascular effects of occupational noise. *Occup Med* 2016;66:10-16.
6. Skogstad M, Johannessen HA, Tynes T et al. Corrigendum Systematic review of the cardiovascular effects of occupational noise. *Occup Med* 2016;66:10-16.
7. Theorell T, Jood K, Järvholm LS et al. A systematic review of studies in the contributions of the work environment to ischaemic heart disease development. *Eur J Public Health* 2016;26:470–77.
8. Dzhambov AM, Dimitrova DD. Occupational noise and ischemic heart disease: A systematic review. *Noise Health*. 2016;18:167-77.
9. Kolstad HA, Stokholm Z, Hansen ÅM et al. Whether noise exposure causes stroke or hypertension is still not known. *BMJ* Online [eLetter] 16 December 2013. http://www.bmj.com/content/347/bmj.f7444.long
10. Davies HW, Teschke K, Kenedy SM et al. Occupational exposure to noise and mortality from acute myocardial infarction. *Epidemiology* 2005;16:25-32.
11. Virkkunen H, Kauppinen T, Tenkanen L. Long-term effect of occupational noise on the risk of coronary heart disease. *Scand J Work Environ Health* 2005;31:291-299.
12. Fujino Y, Iso H, Tamakoshi A, for the JACC study group. A prospective cohort study of perceived noise exposure at work and cerebrovascular diseases among male workers in Japan. *J Occup Health* 2007;49:382-388.
13. Stokholm ZA, Bonde JP, Christensen KL et al. Occupational noise exposure and the risk of stroke. *Stroke* 2013;44:3214-3216.
14. Gopinath B, Thiagalingam A, Teber E, Mitchell P. Exposure to workplace noise and the risk of cardiovascular disease events and mortality among older adults. Prev Med 2011;53:390-394.

15. Dzhambov AM, Dimitrova DD, Tokmakova MP. Association between self-reported occupational noise and the prevalence of stroke: Secondary analysis of the National Health Interview Survey, 2014. Noise Control Engineering Journal. 2016;64:779-788.
16. Basner M, Babisch W, Davis A et al. Auditory and non auditory effects of noise on health. *Lancet* 2014;383:1325-1332.
17. Karasek RA. Job demands, job decision latitude, and mental strain: Implications for job redesign. *Admin Sci Qtrly* 1979;24:285-308.
18. Eller NH, Netterstrøm B, Gyntelberg F et al. Work-related psychosocial factors and the development of ischemic heart disease: a systematic review. *Cardiol Rev* 2009;17:83-97.
19. Kivimäki M, Nyberg ST, Batty GD et al. Job strain as a risk factor for coronary heart disease: A collaborative meta-analysis of individual participant data. *Lancet* 2012;380:1491-1497.
20. Selander J, Bluhm G, Nilsson M et al. Joint effects of job strain and road-traffic and occupational noise on myocardial infarction. *Scand J Work Env Health* 2013;39:195-203.
21. Wilhelmsen L, Berglund G, Elmfeldt D et al. The multifactor primary prevention trial in Goteborg, Sweden. *Eur Heart J* 1986;7:279-288.
22. Harmsen P, Lappas G, Rosengren A et al. Long-term risk factors for stroke: Twenty-eight years of follow-up of 7457 middle-aged men in Göteborg, Sweden. *Stroke* 2006; 37:1663-1667.
23. Torén K, Schiöler L, Söderberg M et al. The association between job strain and atrial fibrillation in Swedish men. *Occup Environ Med* 2015;72:177-180.
24. Sjöström M, Lewné M, Alderling M et al. A job-exposure matrix for occupational noise: Development and validation. *Ann Occup Hyg* 2013;57:774-783.
25. Johnson JV, Stewart W, Hall EM et al. Long-term psychosocial work environment and cardiovascular mortality among Swedish men. *Am J Public health* 1996;86:324-331.
26. Fredlund P, Hallqvist J, Diderichsen F. Psykosocial yrkesexponeringsmatris. *Arbete och Hälsa* 2000;11:1-37 [In Swedish].
27. Torén K, Schiöler L, Giang WK et al. A longitudinal general population-based study of job strain and risk for coronary heart disease and stroke in Swedish men. *BMJOpen* 2014;4:e004355

28. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika* 1994;81:515-526.
29. Kivimäki M, Nyberg ST, Fransson EI et al. Associations of job strain and lifestyle factors with risk of coronary artery disease: A meta-analysis of individual participant data. *Can Med Assoc J* 2013;185:763-769.

- **Contributors**: Rosengren, Torén, Andersson conceptualized, designed and supervised the study. Eriksson helped to conceive the study and drafted the manuscript. Sjöström has participated in developing the job exposure matrix regarding noise. Schiöler performed the statistical analyses. Söderberg critically revised the manuscript. All authors were responsible for the drafting of the manuscript and for the final approval of the manuscript.

- **Funding**: The study was funded by the Swedish Research Council (VR), the Swedish Research Council for Health, Working Life and Welfare (FORTE) and the Swedish Heart and Lung Foundation.

- **Competing interests**: None. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: *no support from any organisation for the submitted work*; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work

- **Ethics statement**: Ethics approval by the Ethics Committee for Medical Research at the University of Gothenburg.

- **Provenance and peer review**: Not commissioned; externally peer reviewed.

- **Data sharing statement**: This is a large general population study which has been followed for many years. There are unpublished data in the dataset. Scientific cooperation around this study is possible by contacting the corresponding author.

STROBE. **A longitudinal study of occupational noise exposure and joint effects with job-strain and risk for coronary heart disease and stroke in Swedish men.** 2017-08-14. Helena Eriksson.

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract YES, page 1 and page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found YES page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported YES page 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses YES page 2 and 5
Methods		
Study design	4	Present key elements of study design early in the paper YES page 2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection YES page 5
Participants	6	*(a)* *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. YES page 5-7 *(b)* *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. YES page 5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. YES page 5-7
Bias	9	Describe any efforts to address potential sources of bias. YES page 13
Study size	10	Explain how the study size was arrived at. YES page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. YES page 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding. YES page 8
		(*b*) Describe any methods used to examine subgroups and interactions. YES page 8
		(*c*) Explain how missing data were addressed. YES page 5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed. YES page 5 *Case-control study*—If applicable, explain how matching of cases and controls was addressed

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses page 8

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. YES page 5
		(b) Give reasons for non-participation at each stage YES page 5
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. YES page 6
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount). YES page 8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time YES page 9,10
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. YES page 8-11
		(*b*) Report category boundaries when continuous variables were categorized. YES page 7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses. YES page 10,11
Discussion		
Key results	18	Summarise key results with reference to study objectives. YES page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. YES page 13, 14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. YES page 14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results. YES page 15
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. YES page 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.